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## Journal of Pediatric Surgery CASE REPORTS

journal homepage: [www.jpascasereports.com](http://www.jpascasereports.com)

## Toxic colitis in a 10 year old girl with Crohn's disease

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## ARTICLE INFO

## Article history:

Received 15 July 2013

Received in revised form

8 August 2013

Accepted 9 August 2013

## Key words:

Toxic colitis

Acute colitis

Severe acute colitis

Toxic megacolon

Crohn's disease

Inflammatory bowel disease

## ABSTRACT

Toxic colitis is a well-described, life-threatening complication of inflammatory bowel disease (IBD). The vast majority of reported cases have been in adults. Limited literature exists describing toxic colitis in children with IBD. Virtually all reported pediatric cases have been in the setting of ulcerative colitis. We present a case of a 10 year old girl with Crohn's disease who was hospitalized because of advanced perianal disease with multiple abscesses and fistulae. During her stay, she developed acute toxic colitis with perforation requiring emergent colectomy. It is essential that clinicians are aware that this catastrophic complication can occur rapidly in the pediatric IBD population to ensure timely and appropriate management.

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Toxic colitis is a severe and life-threatening complication of several inflammatory as well as infectious colitides [1]. Inflammatory bowel disease (IBD) in children is generally associated with a higher rate of severe exacerbations than in adults [2]. Surprisingly little data exists on the incidence and diagnosis of toxic colitis in the pediatric IBD population. Every case reported thus far has been in a child with a primary diagnosis of ulcerative colitis (UC). We present the first case report of toxic colitis in a child with known Crohn's disease (CD).

## 1. Case report

A 10 year old girl with a 2.5 year history of CD presented with abdominal pain, diarrhea, and increasing perineal pain associated with fecal incontinence and purulent drainage per rectum. Her disease had been limited to the colon, rectum and perineum. Recent

colonoscopy had shown stricturing, edema, friability, stellate ulcers and pseudopolyps in the sigmoid colon, and thickening of the rectal wall. In the months prior to admission, she had worsening perineal and abdominal symptoms despite treatment with Asacol, Remicade (5 mg/kg), prednisone (starting at 40 mg/day and tapered), and prolonged metronidazole. On presentation to the pediatric colon and rectal surgery clinic she was afebrile with normal vital signs. Her abdomen was soft and non-tender. Examination of the perineum revealed multiple draining fistulae and fluctuant abscesses with surrounding induration and erythema. Several irregular, wide, ulcerating fissures and swollen skin tags were seen on the perineum and in the anal canal. She was very tender on palpation. She was promptly admitted, intravenous antibiotics (piperacillin/tazobactam – Zosyn and metronidazole) were started, and she was taken to the operating room.

Examination under anesthesia and proctoscopy with minimal insufflation revealed severe ulcerative and stricturing anorectal disease from the anal verge up to 10 cm. There was extensive destruction of the anterior sphincter complex along the path of a rectovaginal fistula and a fistula to a left labial abscess. A posterior anal canal opening through a deep ulcer led to several fistula tracts, a postanal cavity and an ascending cavity above the coccyx. The abscesses were incised, drained and unroofed. A silastic seton was placed through the rectovaginal fistula. She was continued on

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intravenous antibiotics, mesalamine, and methylprednisolone. Because of the severity of her perineal disease, she was scheduled to return to the OR on postoperative day (POD) 2 for examination and further debridement.

Despite initially feeling much better, she developed a fever to 40 °C and became tachycardic to the 140's from a baseline in the 70's early on POD 2. Sepsis due to further perineal infection was suspected. Erect CXR showed no evidence of peritoneal free air. She was taken to the OR urgently. Examination under anesthesia revealed clean perineal wounds and no evidence of undrained cavities. However, copious mucous discharge was pouring out of the rectum. Further examination revealed a distended firm abdomen. An on-table abdominal X-ray showed colonic dilatation but no evidence of free air (Fig. 1A). An intra-abdominal source of acute inflammation and sepsis was suspected. While the patient was still under anesthesia, the situation was discussed with her mother, and laparotomy was recommended. Unfortunately, her mother refused and insisted on additional objective information. The patient was awoken from anesthesia. An urgent computed tomography (CT) scan demonstrated substantial free intra-abdominal air, colonic distention from the cecum to the rectum, and inflammatory changes in the terminal ileum, distal descending colon, sigmoid, and rectum (Fig. 1B). During this time she was aggressively resuscitated and supportively managed, however she remained tachycardic and febrile and developed significant abdominal distention and pain. The white blood cell count rose from 7.7 to 17.7, the C-reactive protein (CRP) increased from 32 to 242, the hematocrit dropped from 38 to 29, and the albumin decreased from 3.7 to 3.4.

Given these findings, we obtained consent to proceed with laparotomy. This revealed a necrotic perforation in the proximal transverse colon with minimal fecal soilage but a large amount of free air. There was severe diffuse Crohn's colitis of the entire colon with marked thickening and narrowing of the mid to proximal sigmoid and dilation of the rest of the colon. There was active disease involving the last 10 cm of the terminal ileum. A total abdominal colectomy was performed along with resection of the diseased terminal ileum and end ileostomy with Hartmann's closure of the rectum. The rectal stump was buried in the subcutaneous tissue at the lower end of the midline incision.

The opened specimen showed findings consistent with Crohn's colitis including ileitis and multiple large mucosal ulcers in the ascending colon and hepatic flexure. There was relatively little

gross disease in the transverse colon, but there were severe linear "rake" ulcers, edema and thickening of the descending and sigmoid colon (Fig. 2A). The necrotic perforation was through one of the deep ulcers at the hepatic flexure (Fig. 2B). Pathologic examination showed transmural chronic and acute inflammation and necrotic ulcers consistent with Crohn's disease. No discrete granulomas were seen.

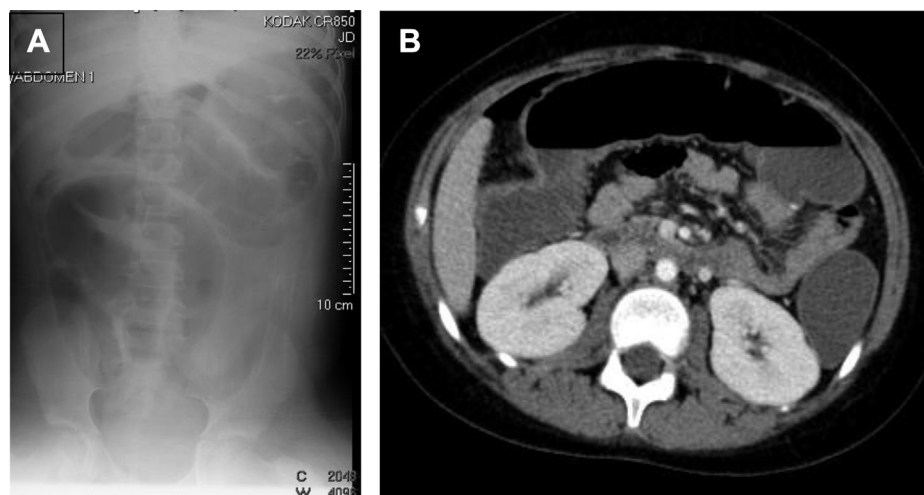
Postoperatively, she progressed well. Her white blood cell count and CRP trended down, and she completed a course of ciprofloxacin and metronidazole. She was discharged on POD 10. After several months of recovery, she adapted to her ileostomy and returned to school full-time. She is maintained on adalimumab and feels better than she has in many years.

A literature search was performed for human studies from 1950 to 2011 on MEDLINE (NLM, National Library of Medicine, Bethesda, MD; 1950–2011). The following terms were searched using the MeSH term and all possible text combinations: acute colitis, toxic colitis, toxic dilatation, toxic megacolon, and Crohn's colitis, ulcerative colitis, pediatrics, children, inflammatory bowel disease. Further articles were found through detailed reference review.

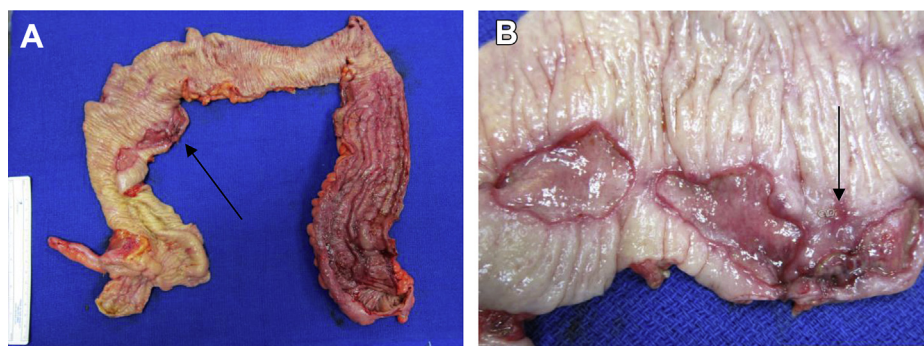
## 2. Discussion

Toxic colitis is a life-threatening condition that is most commonly seen in patients with inflammatory bowel disease. It was first described by Marshak in 1950 as a complication of ulcerative colitis [3]. For over fifteen years it was thought to be specific to UC, until Schachter published the first case report in 1967 of toxic colitis in a patient with Crohn's disease [4]. The incidence of toxic colitis in adults is 1–8% in those presenting to a hospital with Crohn's disease, and 2–21% in those presenting with ulcerative colitis [5–7]. A large retrospective population-based study of children in France found that the incidence of Crohn's disease has been increasing over the last 30 years, with a high rate of extensive, complicated pediatric Crohn's disease resulting in a cumulative probability of surgery in 34% of patients within 5 years of diagnosis [8]. However, only one study reported toxic colitis in pediatric Crohn's, and this was in two patients who had been diagnosed with ulcerative colitis at the time, only developing clear evidence of Crohn's disease years later [9,10].

Prompt recognition of toxic colitis is crucial because the process may lead to bowel perforation, peritonitis and death if not treated rapidly. The incidence of perforation of toxic colitis in a combined



**Fig. 1.** A) Intra-operative supine abdominal X-ray revealing distended loops of bowel but no evidence of free air. B) CT abdomen with intravenous contrast showing dilated colon and free air.



**Fig. 2.** A) Subtotal colectomy specimen, gross showing terminal ileal disease, multiple discrete, deep aphthous ulcers in the right colon, and long, serpiginous rake ulcers in the left colon with skip areas. B) Detail of the ascending colon-hepatic flexure ulcers and the perforation (arrows).

adult inflammatory bowel disease population was found to be high (17–46%) [5,11]. This is important as perforation has been shown to be the most significant predictor of outcome, with mortality as high as 44% vs. 2% without perforation [6]. A further predictor of poor outcome is delay in surgery. Fortunately, in our patient, the condition was promptly recognized and definitively managed with colectomy, without significant delay.

Toxic colitis occurs when the mucosal barrier and immune system are compromised, allowing bacteria to translocate through the walls of the colon and produce systemic symptoms of sepsis [12]. The colonic dilatation is thought to be mediated by both the inhibitory effect of nitric oxide and the inflammation-mediated destruction of myenteric and Auerbach plexuses, reducing colonic muscle tone [13,14]. Although initially described as ‘toxic megacolon,’ it is clear that marked dilation of the colon only occurs in a subset of these patients, and is not necessary for the process to progress to sepsis or perforation. Therefore, it is very important to identify the problem based on clinical and laboratory findings and not on the presence or absence of colonic dilation.

Attempts have been made to standardize the diagnosis of toxic colitis and thereby improve early recognition. In 1969, Jalan proposed the following criteria for adults, notable for the inclusion of colonic dilation [15]. These included 1) radiographic evidence of colonic distention, and 2) at least three subjective criteria which could include fever  $>38^{\circ}\text{C}$ , heart rate  $>120$  beats/min (bpm), neutrophilic leukocytosis  $>10,500/\text{mm}^3$ , and anemia, and 3) at least one factor to include dehydration, altered mental status, electrolyte disturbance, or hypotension [9]. Mid-transverse colon diameter  $>5.5$  cm on abdominal X-ray was also thought to be predictive [16]. In 2009, the Cleveland Clinic Criteria were proposed. This was a much simpler system and did not rely on colonic dilation as a factor. The diagnosis could be made by the presence of any three of the following in the appropriate setting: 1) temperature  $>38^{\circ}\text{C}$ , 2) heart rate  $>100$  bpm, 3) hemoglobin  $<10$  g/dL, 4) white blood cell count  $>10,500/\text{mm}^3$ , and 5) albumin  $<3$  g/dL [17]. Of note, given the absence of colonic dilatation, our patient would have been missed per the Jalan criteria but would have qualified per Cleveland clinic criteria for toxic colitis (4/5 positive). Unfortunately, many of these criteria cannot be directly applied in children because of differences in normal ranges and because of a lack of validation in the pediatric population.

There is a relatively small volume of literature addressing diagnosis of toxic colitis in pediatric IBD, and most refers to patients with ulcerative colitis [18–20]. A retrospective case–control trial of ten children with toxic colitis in the setting of ulcerative colitis showed that fever, tachycardia, dehydration, and electrolyte abnormalities were common, but that altered consciousness and hypotension were not [9]. Significant radiologic findings on abdominal X-rays included

transverse colon lumen diameter  $\geq 56$  mm, air–fluid levels, intestinal thickening, and abnormal colonic haustra. Recent consensus guidelines on acute severe ulcerative colitis in children suggested the following pediatric criteria for toxic colitis: 1) radiographic evidence of transverse colon diameter  $>56$  mm ( $>40$  mm for those  $<10$  yrs old) plus 2) any evidence of systemic toxicity, including fever  $>38^{\circ}\text{C}$ , heart rate  $>2$  standard deviations above the mean for age, dehydration, electrolyte disturbances, altered consciousness, hypotension or shock [21]. Unfortunately, these criteria again include colonic diameter. Despite evidence of systemic toxicity, our 10 year old child with a 42 mm transverse colon diameter would not have been classified as having toxic colitis under these criteria. Use of colonic dilatation alone to guide diagnosis and management in this case would have been an error.

This report is the first to describe an acute severe Crohn’s exacerbation resulting in toxic colitis and perforation in a child. This patient had known Crohn’s colitis that was stable on her immunosuppressive regimen and was only being treated for perianal disease. She developed acute abdominal symptoms soon after a perineal procedure and rapidly progressed to toxic colitis and perforation. Fortunately, she was in the hospital at the time and underwent prompt emergent colectomy. Because of the large adult and pediatric experience at our institution, the problem was identified and treated expeditiously, resulting in a good outcome. This case illustrates the importance of timely and appropriate management of these cases, as well as the understanding that colonic dilation is not necessary for the diagnosis of toxic colitis. We believe that the incidence of this problem will increase along with the increasing incidence of Crohn’s disease in children. It is likely that this complication is under reported in the pediatric population accounting for the paucity of reports in the literature.

### 3. Conclusion

Since its first description in 1950, the clinical syndrome of toxic colitis has become associated with an increasing number of inflammatory and infective colitides. To our knowledge, this is the first case report describing toxic colitis in a child with the diagnosis of Crohn’s disease. As the inflammatory bowel disease phenotype is commonly more severe in the pediatric population, awareness that toxic colitis can manifest in pediatric Crohn’s, does not absolutely present with colonic dilatation, and how its presentation may differ from adults, is essential to preventing delays in diagnosis and treatment of this condition.

### Financial disclosures

None.

**Support**

None.

**Conflict of interest**

None.

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